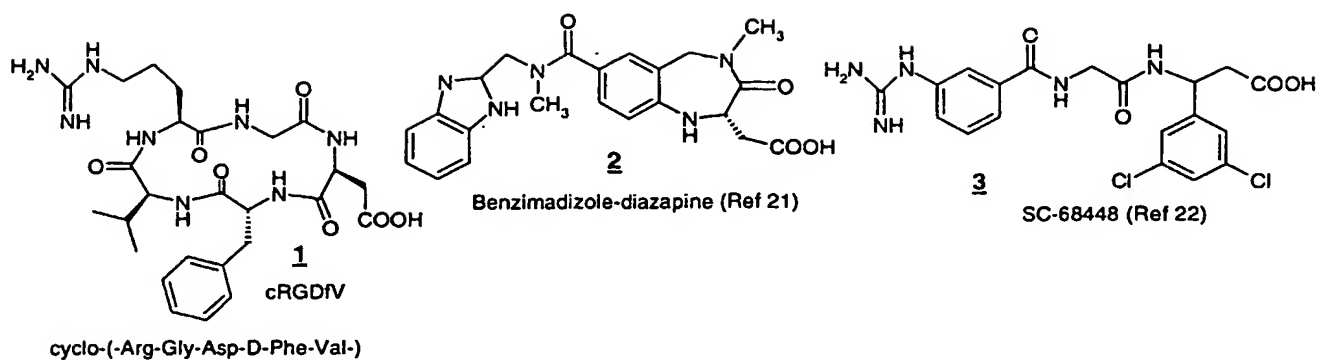
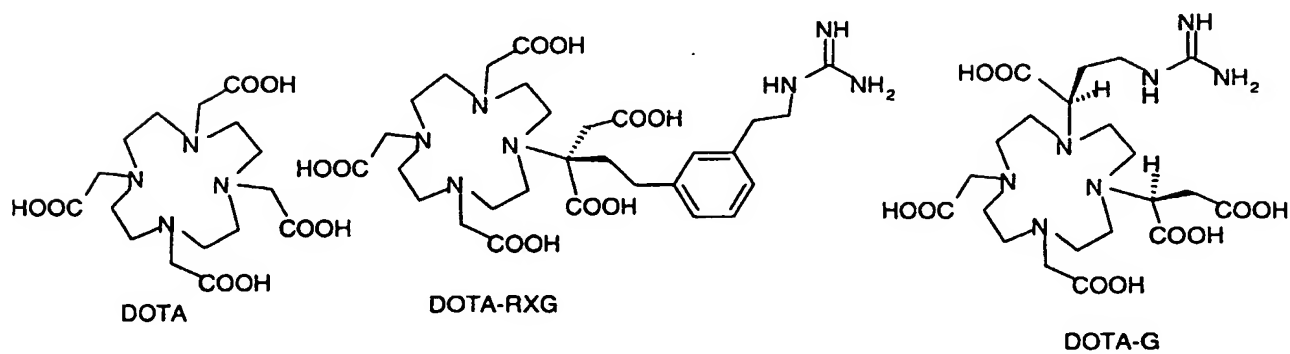
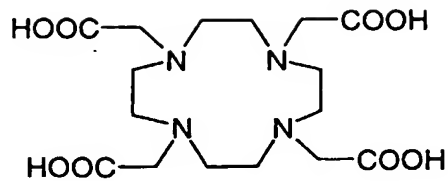
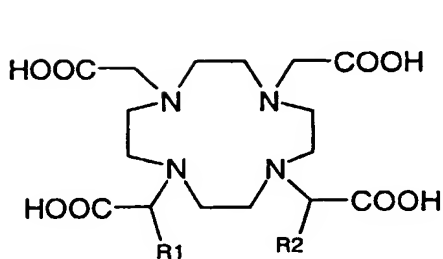
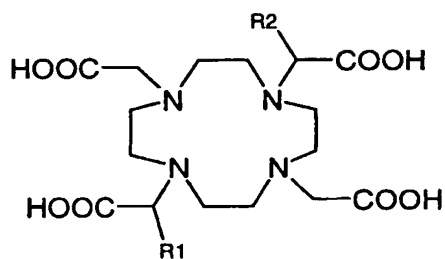
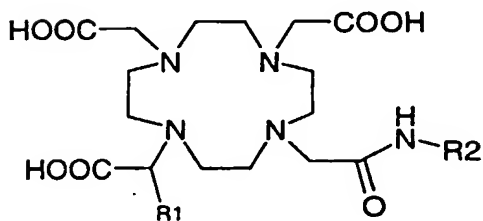
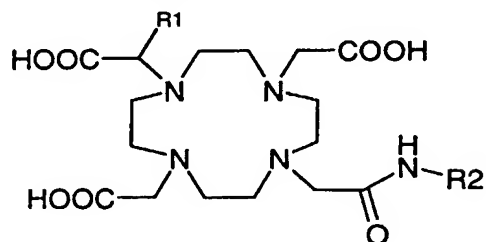


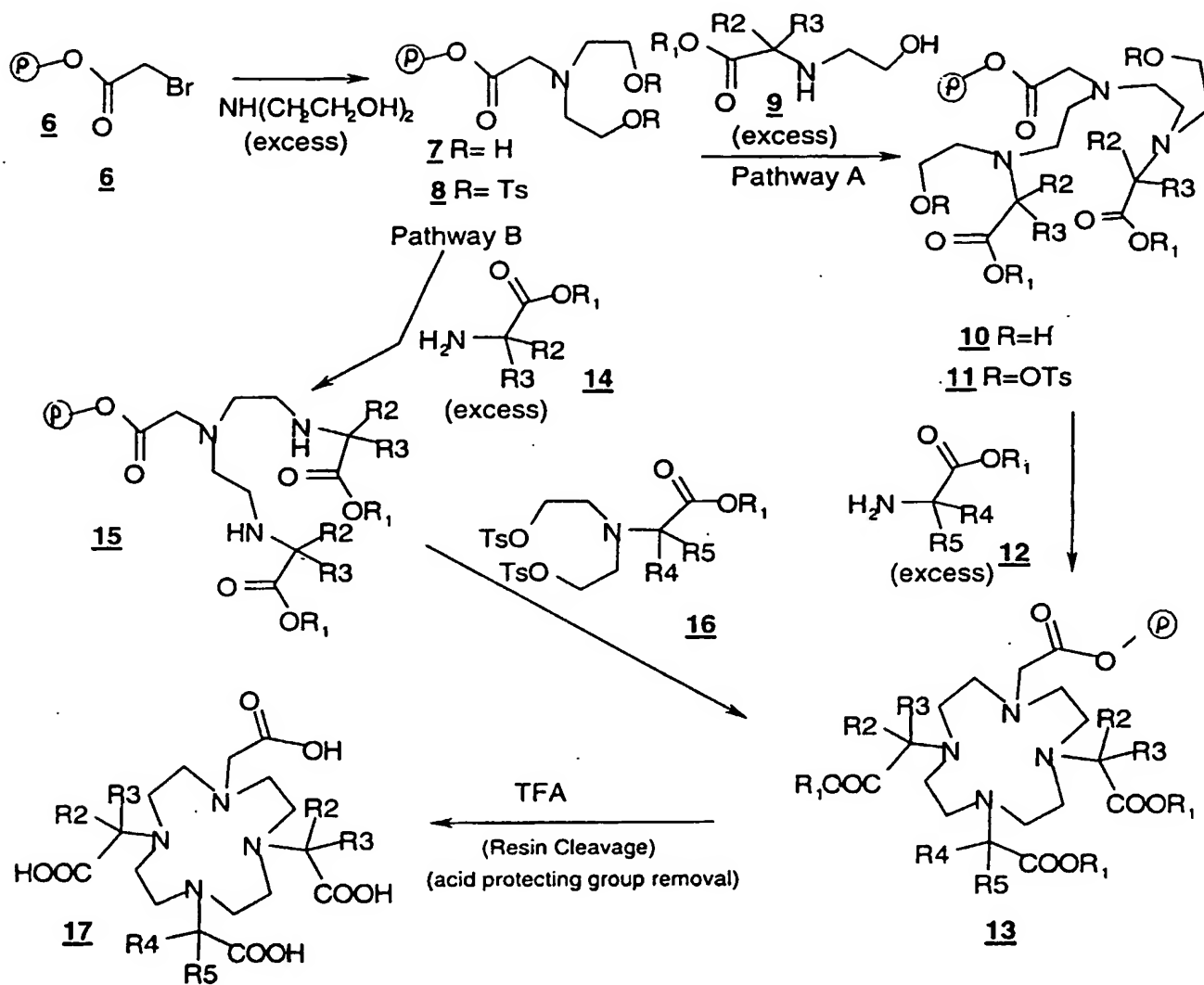
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**Fig. 1****Fig. 2**

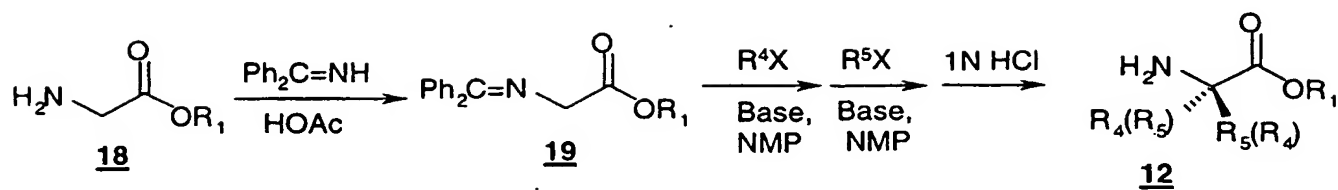
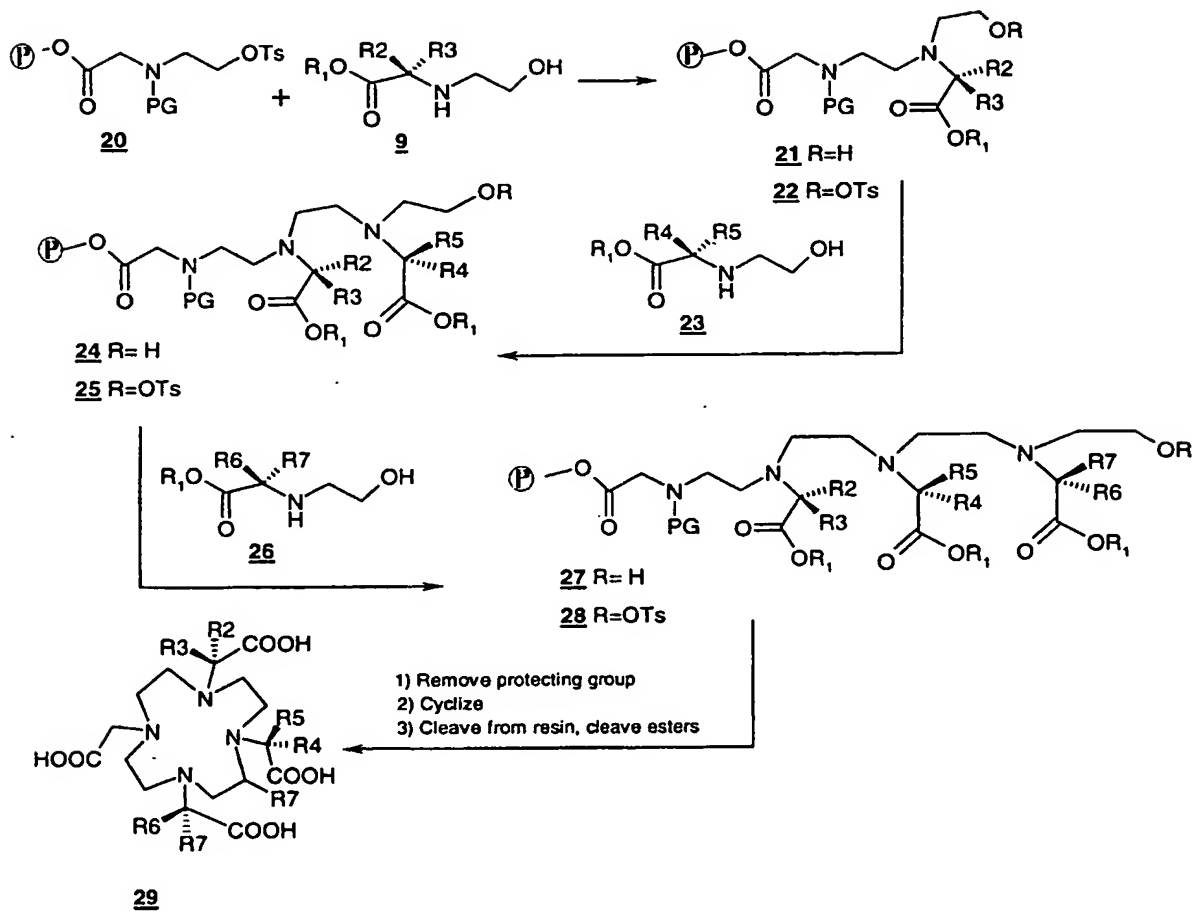
2/13

**DOTA****1,4-alpha substitution****1,7-alpha substitution****1,4-alpha substitution**
DO3A-Amides**1,7-alpha substitution**
DO3A-Amides**Fig. 3**

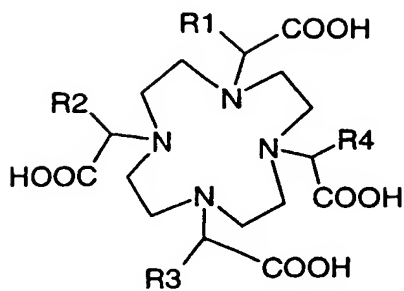
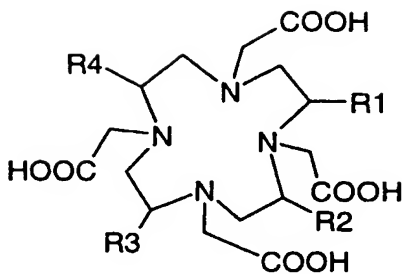
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**Fig. 4**

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**Fig. 5****Fig. 6**

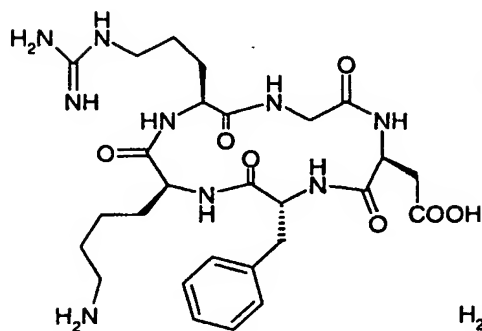
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R1,R2,R3,R4= Z-M

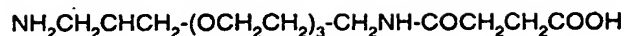
Z= linker/spacer of variable length, shape, flexibility

M= RDG mimic that selectively antagonizes avb3 intetrin

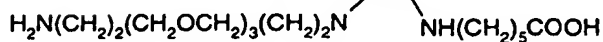
Fig. 732

c(RDGfK)

cyclo-(-Arg-Gly-Asp-D-Phe-Lys-)



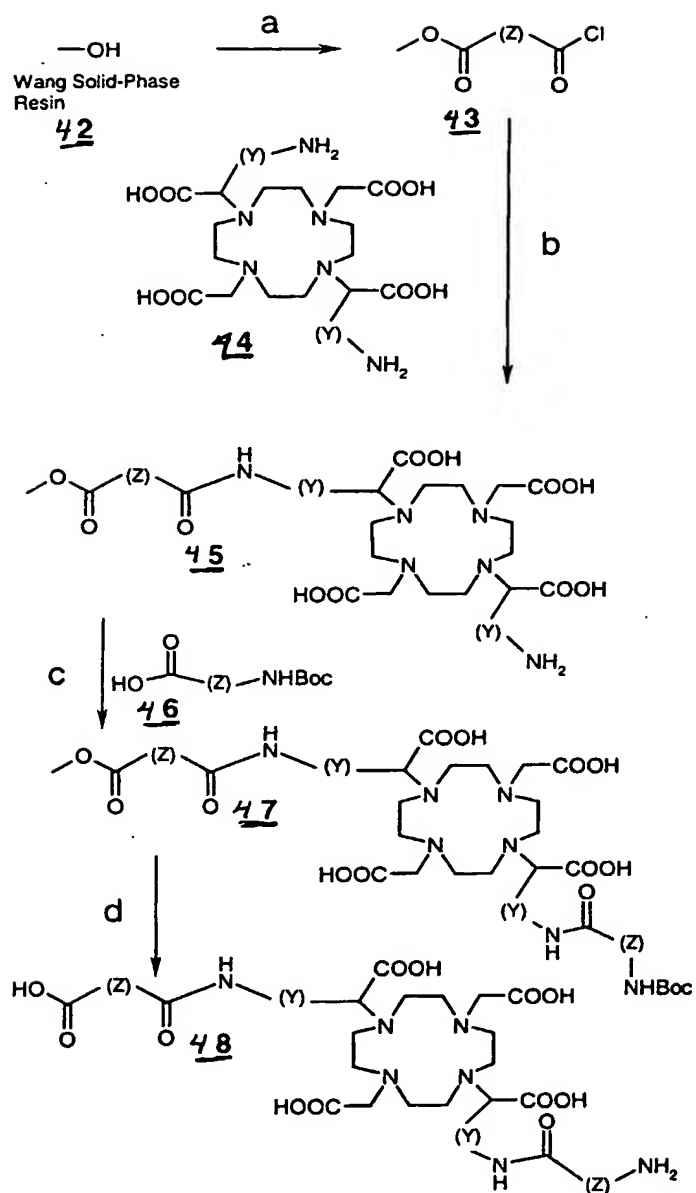
(ref 38)

33

(ref 39)

34**Fig. 8**

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a) symmetrical acid chloride, pyridine, CH₂Cl₂;b) DMF, Et₃N;

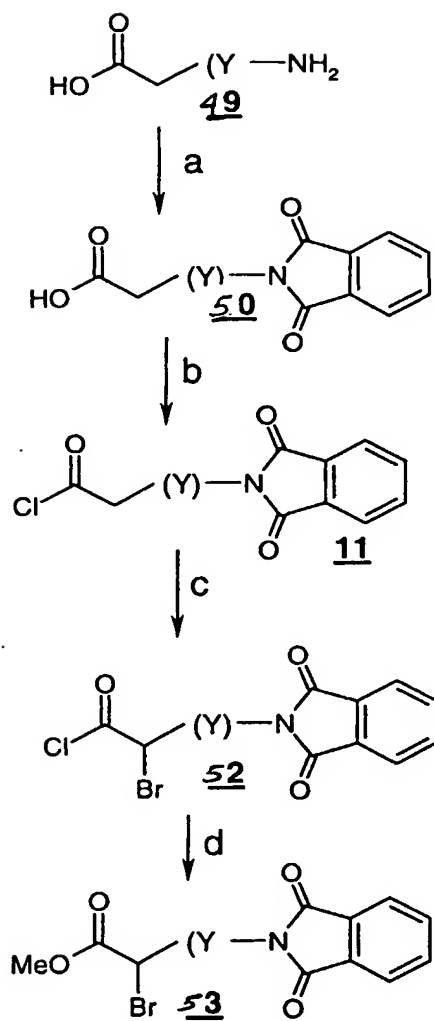
c) carbodiimide coupling or acid chloride;

d) Trifluoroacetic acid/CH₂Cl₂ 50/50

(Y)= 1,2,4 methylene units

(Z)= variable spacer groups

Fig. 9



a) phthalic anhydride, toluene, reflux;
b) thionyl chloride, toluene, reflux;
c) N-Bromosuccinimide, CCl₄, reflux;
d) quench in MeOH
(Y)= 1,2,4 methylene units

Fig. 10

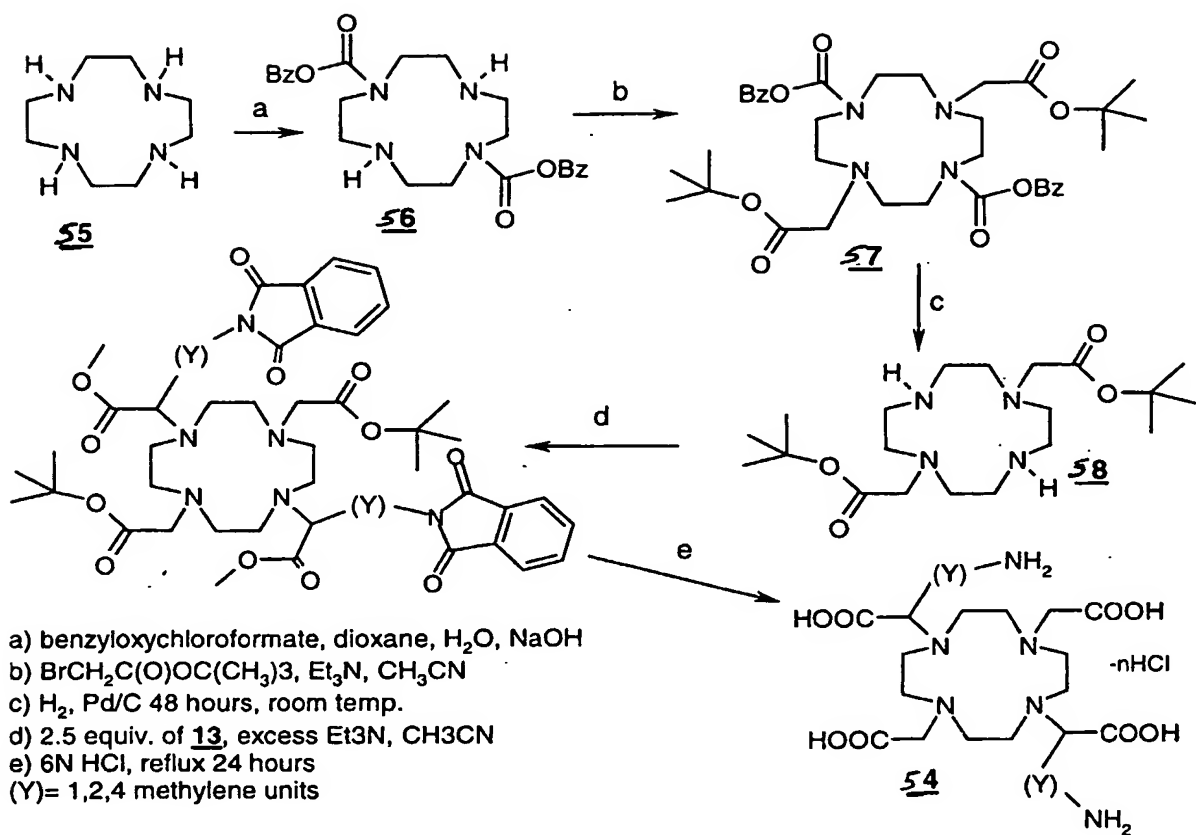


Fig. 11

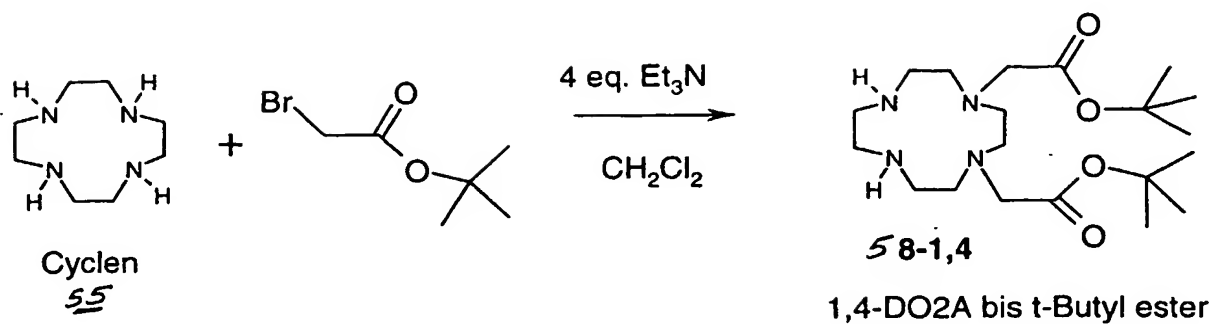


Fig. 12

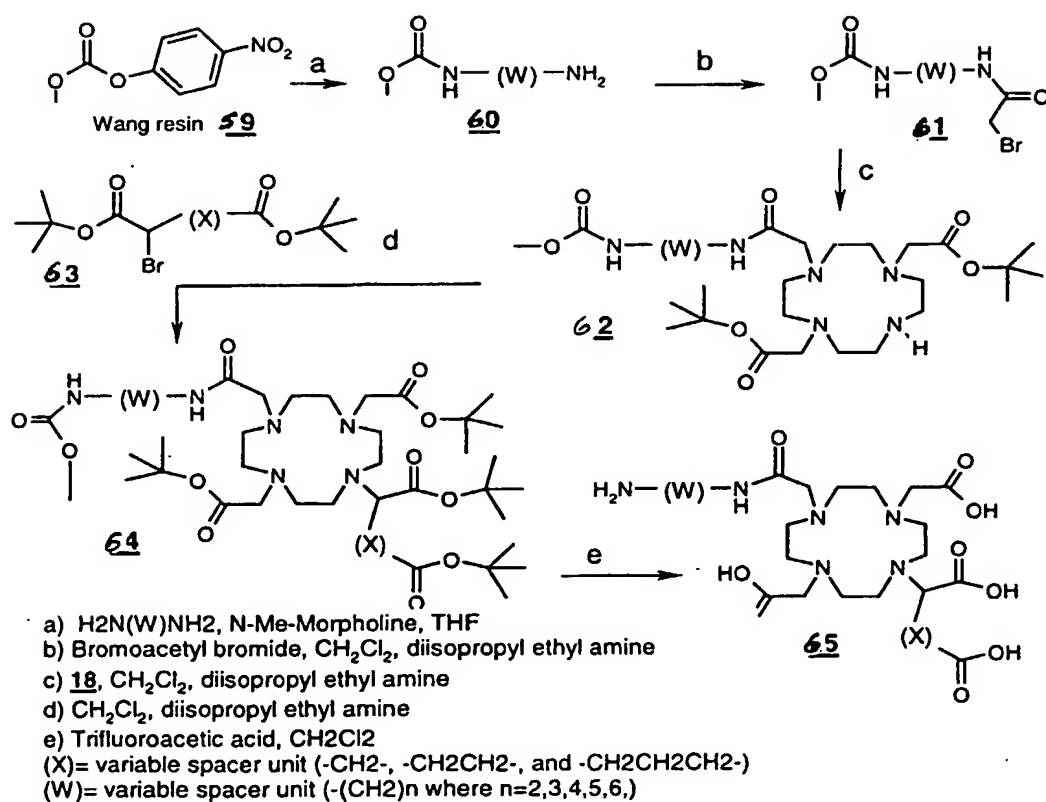
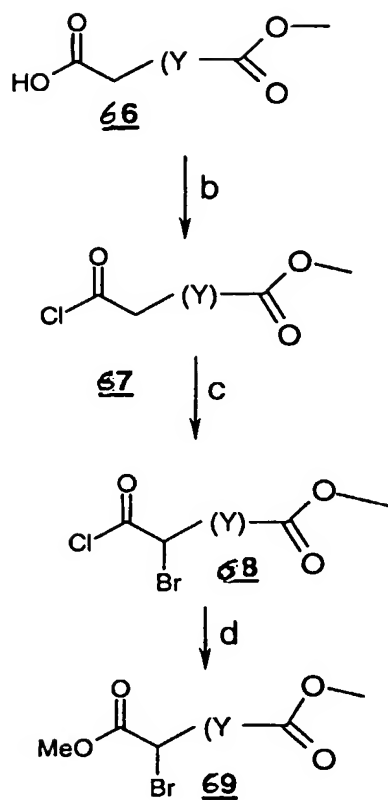


Fig. 13



b) thionyl chloride, toluene, reflux;
 c) N-Bromosuccinimide, CCl₄, reflux;
 d) quench in MeOH
 (Y) = 0 to 4 methylene units

Fig. 14

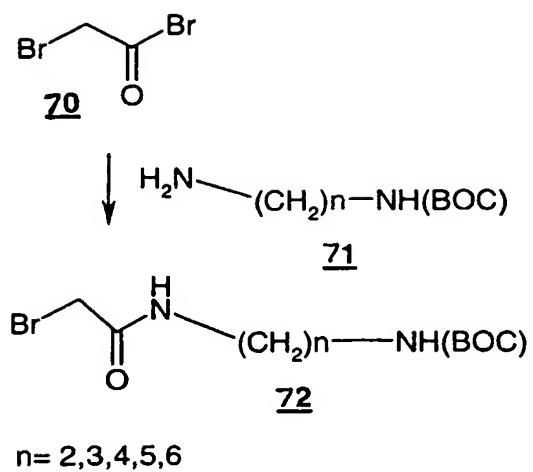
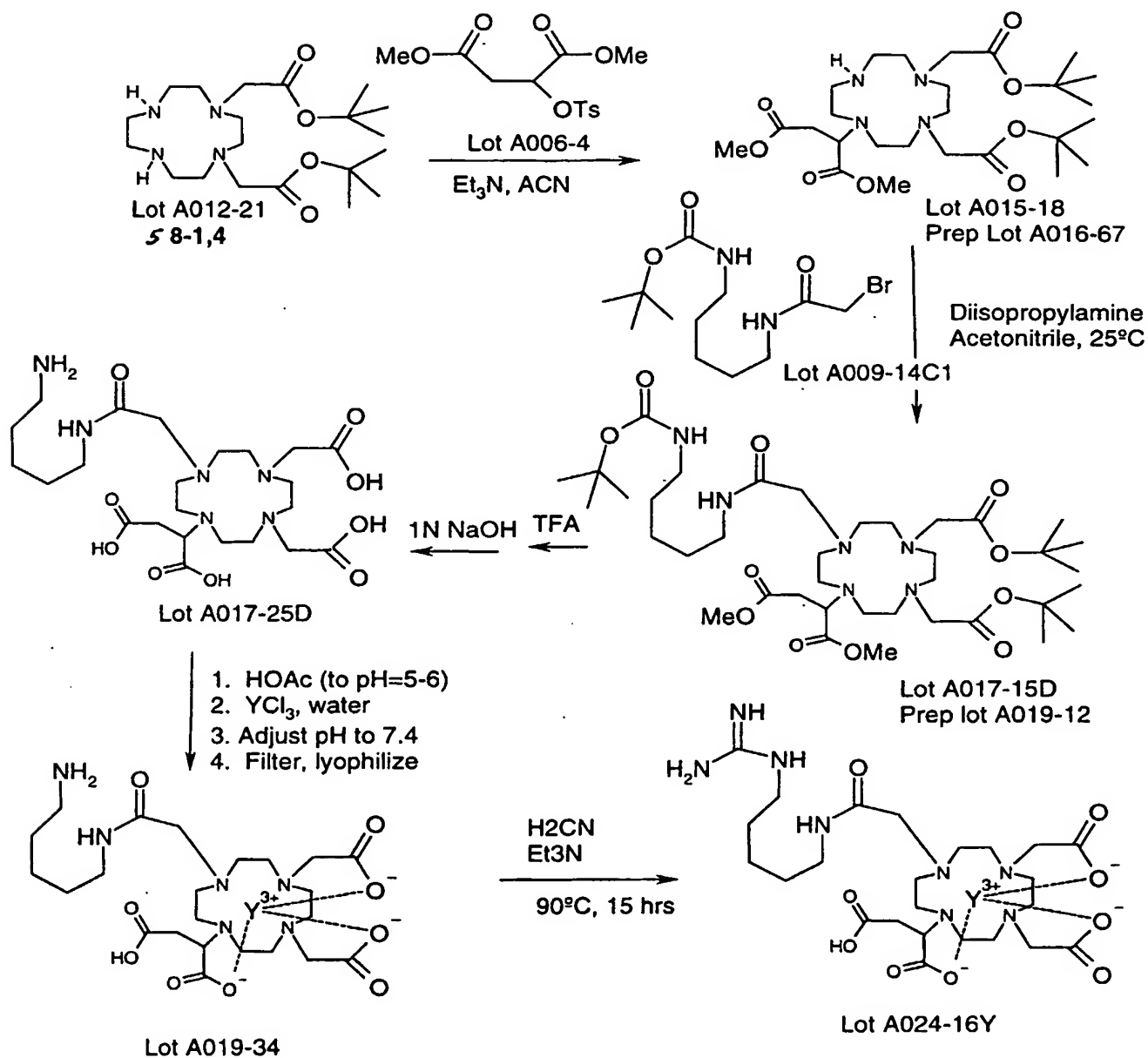
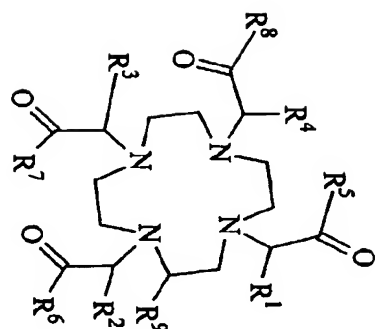


Fig. 15

**Fig. 16**



DOTA Based Species

DOTA Based Species	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	R ⁹
A011-65C	CO ₂ B-CH ₃	H	H	H	OC ₂ H ₅	OH	NH(CH ₂) ₃ NH ₂	-OH	H
A013-17	-(CH ₂) ₂ NH ₂	-(CH ₂) ₂ NH ₂	H	H	-OH	-OH	OH	-OH	H
A017-79J	-(CH ₂) ₂ G	-(CH ₂) ₂ G	H	H	-OH	-OH	-OH	-OH	H
A017-80D	-(CH ₂) ₂ G	H	-(CH ₂) ₂ G	H	-OH	-OH	-OH	-OH	H
A017-80K	-(CH ₂) ₂ G	H	-(CH ₂) ₂ G	H	-OH	-OH	-OH	-OH	H
A007-26	H	-(CH ₂) ₂ S	H	H	-NH(CH ₂) ₆ NH ₂	-OH	OH	-OH	H
A008-43	H	H	H	H	-OH	-OH	OH	-OH	-CH ₂ -A-NH ₂ -(CH ₂) ₂ -NH ₂
A012-17	H	-(CH ₂) ₂ S	H	H	-NH(CH ₂) ₆ NH ₂	-OH	OH	-OH	H
A012-19	H	-(CH ₂) ₂ S	H	H	-NH(CH ₂) ₆ NH ₂	-OH	OH	-OH	H
A013-75 (B-E)	H	-CH ₂ CO ₂ H	H	H	-NH(CH ₂) ₆ NH ₂	-OH	OH	-OH	H
A013-50 (A-D)	H	-CH ₂ CO ₂ H	H	H	-NH(CH ₂) ₆ -G n=3-6	-OH	-OH	-OH	H
A017-21 (A-E)	-(CH ₂) ₂ CO ₂ H	H	H	H	-OH	-NH(CH ₂) ₆ NH ₂ n=2-6	OH	-OH	H
A017-25 (A-E)	-CH ₂ CO ₂ H	H	H	H	-OH	-NH(CH ₂) ₆ NH ₂ n=2-6	OH	-OH	H
A022-16 (Q-U)	-(CH ₂) ₂ CO ₂ H	H	H	H	-OH	-NH(CH ₂) ₆ -G n=2-6	OH	-OH	H
A024-16 (V-Z)	-CH ₂ CO ₂ H	H	H	H	-OH	-NH(CH ₂) ₆ -G n=2-6	OH	-OH	H

Fig. 17

DOTA Based Species	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	R ⁹
A011-97 (A-E)	-(CH ₂) ₂ CO ₂ H	H	H	H	-OH	-OH	NH(CH ₂) _n NH ₂ n = 2-6	-OH	H
A011-97 F	-CH ₂ CO ₂ H	H	H	H	-OH	-OH	NH(CH ₂) ₂ NH ₂	-OH	H
A013-67(A-E)	-(CH ₂) ₃ CO ₂ H	H	H	H	-OH	-OH	-NH(CH ₂) _n NH ₂ n = 2-6	-OH	H
A017-79 (E-H)	-(CH ₂) ₂ CO ₂ H	H	H	H	-OH	-OH	-NH(CH ₂) _n G n = 2-6	-OH	H
A016-46	-(CH ₂) ₃ CO ₂ H	H	H	H	-OH	-OH	-NH(CH ₂) ₂ NH ₂	-OH	H
A024-16 (M-P)	-(CH ₂) ₃ CO ₂ H	H	H	H	-OH	-OH	-NH(CH ₂) _n G n = 3-6	-OH	H
A013-77	-(CH ₂) ₂ NH ₂	H	-(CH ₂) ₃ CO ₂ H	H	-OH	-OH	OH	-OH	H
A013-79	-(CH ₂) ₄ NH ₂	H	-(CH ₂) ₃ CO ₂ H	H	-OH	-OH	OH	-OH	H
A008-59	H	-(CH ₂) ₂ NH ₂	H	-(CH ₂) ₂ NH ₂	-OH	-OH	OH	-OH	H
A011-35	(CH ₂) ₂ NH ₂	(CH ₂) ₂ NH ₂	H	H	-OH	-OH	-OH	-OH	H
A017-79D	-(CH ₂) ₂ G	H	-(CH ₂) ₂ G	H	-OH	-OH	OH	-OH	H
A013-19	-(CH ₂) ₄ NH ₂	H	-(CH ₂) ₂ NH ₂	H	-OH	-OH	OH	-OH	H
A017-79 (B-C)	H	H	H	H	-OH	-OH	OH	-OH	ANH(CH ₂) _n G n = 2, 4
A008-43	H	H	H	H	-OH	-OH	-OH	-OH	ANH(CH ₂) ₂ NH ₂
A007-29	H	H	H	H	-OH	-OH	OH	-OH	ANH(CH ₂) ₄ NH ₂

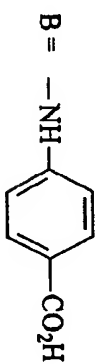
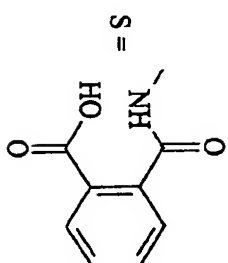
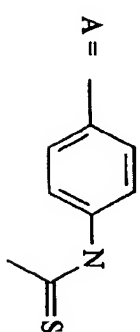


Fig. 17